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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/543,771	04/05/2000	John P. Carulli	032796-014	6685

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EXAMINER
KAUSHAL, SUMESH

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 11/22/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action

Application No.	Applicant(s)	
09/543,771	CARULLI ET AL.	
Examiner	**Art Unit**	
Sumesh Kaushal Ph.D.	1636	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 28 October 2002 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☒ The period for reply expires *4* months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on _____. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2. ☒ The proposed amendment(s) will not be entered because:

   (a) ☒ they raise new issues that would require further consideration and/or search (see NOTE below);

   (b) ☐ they raise the issue of new matter (see Note below);

   (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

   (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: *See Continuation Sheet*.

3. ☐ Applicant's reply has overcome the following rejection(s): _____.

4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5. ☒ The a)☐ affidavit, b)☐ exhibit, or c)☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: *See Continuation Sheet*.

6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7. ☐ For purposes of Appeal, the proposed amendment(s) a)☒ will not be entered or b)☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

   The status of the claim(s) is (or will be) as follows:

   Claim(s) allowed: *1*.

   Claim(s) objected to: *none*.

   Claim(s) rejected: *14-19 and 26-29*.

   Claim(s) withdrawn from consideration: *none*.

8. ☐ The proposed drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.

9. ☐ Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). _____.

10. ☐ Other: _____

Attachment to the Advisory Action (PTO-303)

Continuation of 2. NOTE: Claim limitation "biologically active fragment thereof" would require further consideration under 35 USC 112(2) regarding indefinite language. claim limitation "an isolated amino acid sequence comprising the extra cellular domain of the amino acid of SEQ ID NO:4" would require further consideration under 35 USC 102 regarding prior art issues

Continuation of 5. does NOT place the application in condition for allowance because: Claims 14-19 and 26-29 stand rejected under 35 U.S.C. 112, first paragraph regarding enable issues for the same reasons of record as set forth in the office action mailed on 06/26/02.
Applicant's arguments filed on 10/28/02 have been fully considered but they are not persuasive. The applicant argues that the specification is enabled for the method of altering bone development and treatment. The applicant further argues that applicant is not required to submit role of SEQ ID NO:4 in bone development and/or osteoporosis. The applicant further argues that there is no evidence that any similarity between LRP5 and HBM would eliminate the role of HBM protein in bone development. The applicant concluded that the instant specification need not to specify the dosage or method of use it is know that one skill in the art could obtain. However, this is not found unpersuasive because applicant fails to consider the earlier office action its entirety, which clearly provided evidence why the invention as claimed is not enabled. The scope of the invention as claimed encompasses a method of altering bone development in a host comprising administering the amino acid of SEQ ID NO:4 to a Somatic cell and/or Germ-line cell of the host. In addition the scope of invention as claimed encompasses a method of treating osteoporosis which comprises administering the i) amino acid of SEQ ID NO:4 , ii) the extracellular domain of the amino acid of SEQ ID NO:4 and iii) intracellular domain of the amino acid of SEQ ID NO:4. The specification even fails disclose the role of HBM in any signal transduction pathway, that leads to bone development Considering the multifactorial nature of bone development and osteoporosis, the instant specification fails to provide a single working example that establishes that the administration of i) HBM (SEQ ID NO:4) ii) the extracellular domain of HBM or iii) intracellular domain HBM leads to bone development and/or the treatment of osteoporosis in any and all vertebrates (see pages 4-7 of office action mailed on 6/26/02). Furthermore, considering the high amino acid sequence homology (99.6%) between SEQ ID NO:4 and LDL-receptor the specification fails to provide any guidance as how one skill in the art would specifically target the membrane of bone cells in vivo so that the administered HBM-receptor takes over the endogenous Zmax1 functions (see pages 5-6 of office action mailed on 6/26/02). Similarly, the specification fails to provide any evidence that the administration of interacellular domain in vivo would modify the interacellular signal transduction of bone cells, which result in HBM phenotype. Furthermore, the administration of extracellular domain alone would be non-productive as it only completes with a natural ligand for HBM receptor protein (i.e. LDL). The specification even fails to disclose any other natural ligand for the extracellular domain of HBM-receptor protein, blocking of which regulates the bone formation. At best the only known ligand for thee SEQ ID NO: 4 would be LDL and the specification fails to provide any evidence that bone development and or osteoporosis could be regulated by blocking LDL activity. Therefore, one skill in the art would have to engage in excessive and undue amount of experimentation to exercise the invention as claimed.

Scott D. Priebe

SCOTT D. PRIEBE
PRIMARY EXAMINER